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EXAMINER	
CHERNYSHEV, OLGA N	
ART UNIT	PAPER NUMBER
1646	12

DATE MAILED: 07/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/831,754	NITSCH ET AL.	
	Examiner	Art Unit	
	Olga N. Chernyshev	1646	

-- The MAILING DATE of this communicati n appears on the cover she t with the correspondence address --

Peri d for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *39-76* is/are pending in the application.

4a) Of the above claim(s) *55-76* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I in Paper No. 9 is acknowledged. The traversal is on the ground(s) that "the restriction incorrectly states that Group I includes claims 39-54 claiming "a method of producing a new nucleic acid". There are no method claims among claims 39-54" (page 1 of the Response). This is not found persuasive because Group I includes claims 39-45, drawn to an isolated nucleic acid molecule, which represents first recited product in accordance with 37 C.F.R. § 1.475 (d), claims 46-51, drawn to a vector and a host cell, which encompass a first method of using of the nucleic acid, or a method of producing a protein, and, finally claims 52-54, drawn to a protein, which encompasses a product produced by using a nucleic acid of the instant invention. Therefore, "the first method of using the nucleic acid" (see bottom at page 1 of the Response) is included within the claims of Group I .

The requirement is still deemed proper and is therefore made FINAL.

Claims 55-76 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 9.

Claims 39-54 are under examination in the instant office action.

Sequence compliance

2. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. § 1.821 through

1.825. Specifically, no sequence listing has been provided which includes the nucleotide sequences presented on page 31 of the instant specification. In case these sequences are new, Applicant needs to provide a substitute computer readable form (CRF) copy of a "Sequence Listing" which includes all of the sequences that are present in the instant application and encompassed by these rules, a substitute paper copy of that "Sequence Listing", an amendment directing the entry of that paper copy into the specification, and a statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. §§ 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d). The instant specification will also need to be amended so that it complies with 37 C.F.R. § 1.821(d) which requires a reference to a particular sequence identifier (SEQ ID NO:) be made in the specification and claims wherever a reference is made to that sequence. For rules interpretation Applicant may call (703) 308-1123. See M.P.E.P. 2422.04.

Priority

3. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Drawings

4. Figures 14 and 15 of the instant application are presented on separate pages or in separate panels. 37 C.F.R. § 1.84(u) (1) states that when partial views of a drawing which are intended to form one complete view, whether contained on one or several sheets, must be identified by the same number followed by a capital letter. For example, the three pages of Figure 14 in the instant

specification should be renumbered "Figure 1A" – "Figure 14C". Applicant is reminded that once the drawings are changed to meet the separate numbering requirement of 37 C.F.R. § 1.84(u) (1), the specification should be amended to change the Brief Description of the Drawings and the rest of the specification to refer to each Figure accordingly. If, for example, Figure 1 is divided into Figures 14A-14C, then the Brief Description and all the references to this figure in the specification must refer to this Figure in the same manner.

Specification

5. The text of the instant specification is not in compliance with the requirements for Sequence Identifiers (see MPEP 2422.03). The appropriate format for sequence identifiers is SEQ ID NO: X, wherein "X" is the sequence number. Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. Claims 52-54 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claims fail to include any limitations which would distinguish the claimed proteins, peptides and compositions from those which occur in nature. In the absence of the hand of man, naturally occurring nucleic acid molecules and proteins are considered non-statutory subject matter. Diamond v. Chakrabarty, 206 USPQ 193 (1980). Additionally, mere purity of a

naturally occurring product does not necessarily impart patentability. Ex parte Siddiqui, 156 USPQ 426 (1966). However, when purity results in a new utility, patentability is considered. Merck Co. v. Chase Chemical Co., 273 F. Supp. 68 (1967). Filing of evidence of a new utility imparted by the increased purity of the claimed invention and amendment of the claims to recite a purity limitation, if supported by the specification, is suggested to obviate this rejection. Applicant should point to the basis in the specification for any amendment to the claims.

7. Claims 39-54 are rejected under 35 U.S.C. 101 because the claimed invention is drawn to an invention with no apparent or disclosed specific and substantial credible utility. The instant application has provided a description of an isolated DNA encoding a protein and the protein encoded thereby. The instant application does not disclose a specific biological role for this protein or its significance to a particular disease, disorder or physiological process, which one would wish to manipulate for a desired clinical effect.

It is clear from the instant application that the protein described therein is what is termed an "orphan protein" in the art. The DNA of the instant application has been isolated because of its similarity to a known DNA. There is little doubt that, after complete characterization, this DNA and encoded protein may be found to have a specific and substantial credible utility. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are

"useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an immediate obvious or fully disclosed "real world" utility. The court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion".

The instant claims are drawn to an isolated nucleic acid molecule and the protein encoded thereby designated as Seladin-1 of SEQ ID NO: 1. It is asserted in the instant specification that "[o]ne function of SELADIN-1 is to protect cells against degeneration and cell death" (page 2, last paragraph, of the instant specification). The results of the analysis of tissue samples of normal individuals and Alzheimer's patients revealed that Seladin-1 is expressed throughout the human brain (page 21-22, Figure 5) and also in other human tissues (page 22, Figure 6). Furthermore, the transcripts levels of Seladin-1"were significantly lower in brain regions with severe neurodegeneration" (page 21, Figure 4) and in particular "[I]n AD brains, the expression of SELADIN-1 was substantially lower in the inferior temporal lobe compared to the frontal cortex" (page 25-26, Figures 17 and 18). The instant specification also describes the results of experiments where human H4 neuroglioma cells were transfected with *Seladin-1* and exposed to H_2O_2-induced oxidative stress, which resulted in better resistance of the cells against induction of cell death. Thus, based on the presented data, it is asserted that Seladin-1 "is an integral component of the cellular machinery protecting cells, in particular neurons" (page 30, of the instant specification).

One skilled in the art readily understands that many proteins are differentially expressed in the areas of neuronal degeneration within Alzheimer's disease brain as compared to normal control. Based on the fact that Seladin-1 has lower levels of expression in brain regions with severe neurodegeneration one would not reasonably conclude that biological function of Seladin-1 is related to its protective role against degeneration and cell death in general, as asserted in the instant specification. Furthermore, because it appears that overexpression of Seladin-1 leads to the increased protection of cells against oxidative stress *in vitro*, it is asserted that biological significance of Seladin-1 is to protect cells against oxidative stress. However, it is not clear and not explained in the instant specification how this asserted biological function of the instant nucleic acid encoding Seladin-1 supports its practical, "real world" utility. The instant specification fails to provide any evidence or sound scientific reasoning that administration of Seladin-1 proteins, for example, would have protective effect against degeneration and lead to protection of cells against oxidative stress and associated with it cell death. Similarly, the practical specific and substantial utility of the DNA encoding Seladin-1 is also not disclosed.

According to the instant specification, "SELADIN-1 is a good candidate gene for therapeutical intervention to protect cells against degeneration and cell death. It is in particular, a good candidate gene for therapeutical intervention to protect neurons from Aβ induced cytotoxicity" (page 30). However, 35 USC § 101 clearly states that the invention must be useful in currently available form, which precludes any further experimentation to establish the utility of the claimed invention. To accept the assertion of utility of Seladin-1 as "a good candidate gene for therapeutical intervention to protect cells against degeneration and cell death" would be equivalent to accepting the fact that the instant invention was not completed, as filed, because it

clearly requires further research to determine how to manipulate the claimed DNA in order to achieve the desired clinical effect, such as treatment of Alzheimer's disease, for example. However, this further research has been determined by the courts to be a utility, which, alone, does not support patentability.

Since the instant specification does not disclose a credible "real world" use for the instant nucleic acid and encoded protein I their currently available form, then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. § 101 as being useful.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-2 and 4 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a clear asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

9. Claims 40, 45 and 53 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 40 and 53 are directed to a functional variant of a nucleic acid molecule encoding a protein of SEQ ID NO: 1, the function of which is to protect cells against degeneration and/or

cell death. Claim 45 depends from claim 40. However, the instant specification fails to describe the entire genus of proteins which are encompassed by these claims. In making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, it is necessary to understand what Applicant has possession of and what Applicant is claiming. From the specification, it is clear that Applicant has possession of a nucleic acid molecule which encodes a protein which has the amino acid sequence of SEQ ID NO: 1. This nucleic acid molecule has a nucleic acid sequence of SEQ ID NO: 2. The subject matter which is claimed is described above. First, a determination of the level of predictability in the art must be made in that whether the level of skill in the art leads to a predictability of structure; and/or whether teachings in the application or prior art lead to a predictability of structure. The claims are functional variants of a nucleic acid molecule encoding a protein of SEQ ID NO: 1, the function of which is to protect cells against degeneration and/or cell death. First, the claims are not limited to a nucleic acid molecule with a specific nucleic acid sequence. The claims only require the polynucleotide to share some degree of structural similarity to the isolated nucleic acid of SEQ ID NO: 2. The specification only describes a nucleic acid molecule having the nucleic acid sequence of SEQ ID NO: 2 and fails to teach or describe any other polynucleotide which lacks the nucleic acid sequence of SEQ ID NO: 2 and encodes the protein, the function of which is to protect cells against degeneration and/or cell death has the activities possessed by the isolated protein. Therefore, there is a lack of guidance or teaching regarding structure and function because there is only a single example provided in the specification and because there is no guidance found in the prior art.

Next in making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, each claimed species and genus must be evaluated to determine whether there is sufficient written description to inform a skilled artisan that applicant was in possession of the claimed invention at the time the application was filed. With this regard, the instant application fails to provide a written description of the species or the genus which are encompassed by the instant claims except for the polynucleotide of SEQ ID NO: 2. The specification does not provide a complete structure of those functional variants of a nucleic acid molecule encoding a protein of SEQ ID NO: 1, the function of which is to protect cells against degeneration and/or cell death. The claims also fail to recite other relevant identifying characteristics (physical and/or chemical and/or functional characteristics coupled with a known or disclosed correlation between function and structure) sufficient to describe the claimed invention in such full, clear, concise and exact terms that a skilled artisan would recognize applicant was in possession of the claimed invention. The specification fails to provide a representative number of species for the claimed genus (those functional variants of a nucleic acid molecule encoding a protein of SEQ ID NO: 1, the function of which is to protect cells against degeneration and/or cell death) because the specification teaches only the one embodiment of SEQ ID NO: 2. Therefore, the claims are directed subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 42-44 and 49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

11. Regarding claim 42, the phrase " in particular " renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

12. Claim 43 is indefinite and ambiguous for recitation of hybridization "under stringent conditions". Without providing a precise set of hybridization conditions, in the claim or the specification, the metes and bounds of the claimed isolated nucleic acid molecule cannot be defined.

13. Claim 49 recites the limitation "a plasmid" in claim 46. There is insufficient antecedent basis for this limitation in the claim.

14. Claim 44 is indefinite for being dependent form indefinite claim.

Conclusion

15. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (703) 305-1003. The examiner can normally be reached on Monday to Friday 9 AM to 5 PM ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (703) 308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 782-9306 for regular communications and (703) 782-9307 for After Final communications.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)0. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 308-4556 or (703) 308-4242. If either of these numbers is out of service, please call the Group receptionist for an alternative number. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. Official papers should NOT be faxed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Olga N. Chernyshev, Ph.D.
July 2, 2003

JOHN ULM
PRIMARY EXAMINER
GROUP 1800